

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

Claim 1 (currently amended): A method of reducing the risk of cataract development in a mammal comprising administering to the mammal an effective amount of a non-antimicrobial tetracycline derivative.

Claim 2 (cancelled).

Claim 3 (original): A method according to Claim 1, wherein said tetracycline derivative is a dedimethylaminotetracycline.

Claim 4 (original): A method according to Claim 3, wherein said dedimethylaminotetracycline is selected from the group consisting of 4-dedimethylaminotetracycline, 4-dedimethylamino-5-oxytetracycline, 4-dedimethylamino-7-chlorotetracycline, 4-hydroxy-4-dedimethylaminotetracycline, 5a,6-anhydro-4-hydroxy-4-dedimethylaminotetracycline, 6  $\alpha$  -deoxy-5-hydroxy-4-dedimethylaminotetracycline, 6-demethyl-6-deoxy-4-dedimethylaminotetracycline, 4-dedimethylamino-12a-deoxytetracycline, 12 $\alpha$  -deoxy-4-deoxy-4-dedimethylaminotetracycline, 12a, 4  $\alpha$  -anhydro-4-dedimethylaminotetracycline, 7-dimethylamino-6-demethyl-6-deoxy-4-dedimethylaminotetracycline, 5-hydroxy-6- $\alpha$  -deoxy-4-dedimethylaminotetracycline, 4-dedimethylamino-12  $\alpha$  -deoxyanhydrotetracycline and 4-dedimethylamino-11-hydroxy-12a-deoxytetracycline.

Claim 5 (original): A method according to Claim 1, wherein said tetracycline derivative is 6  $\alpha$  -deoxy 5-hydroxy 4-dedimethylamino tetracycline.

Claim 6 (original): A method according to Claim 1, wherein said tetracycline derivative is selected from the group consisting of 6a-benzylthiomethylenetetracycline, tetracyclino-trile, the mono-N-alkylated amide of tetracycline, 6-fluoro-6-demethyltetracycline, 11a-chlorotetracycline, tetracycline pyrazole, and 12a-deoxytetracycline and its derivatives.

Claims 7-10 (cancelled).

Claim 11 (original): A method according to Claim 1, wherein said tetracycline derivative is administered systemically.

Claim 12 (original): A method according to Claim 11, wherein said tetracycline derivative is administered systemically by a controlled release delivery system.

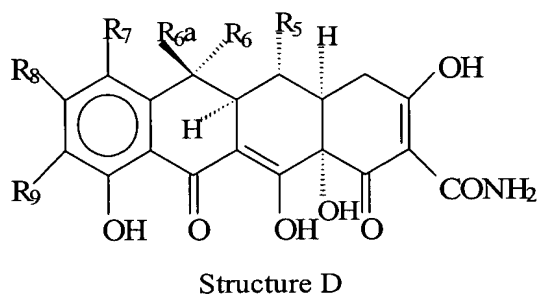
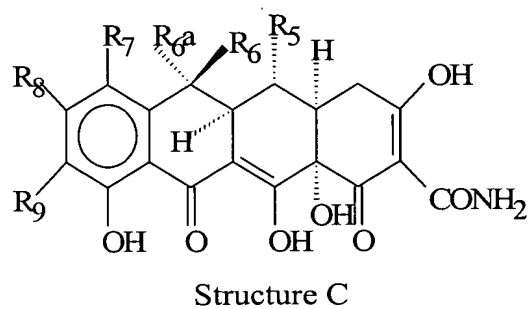
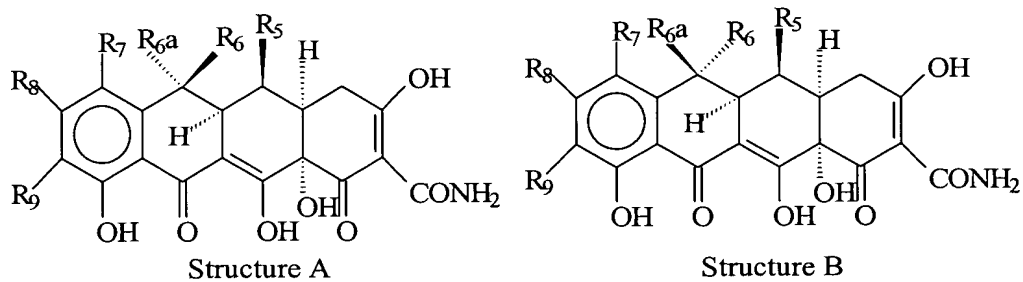
Claim 13 (original): A method according to Claim 1, wherein said tetracycline derivative is administered orally.

Claim 14 (original): A method according to Claim 1, wherein said tetracycline derivative is administered topically.

Claim 15 (currently amended): A method according to Claim 1, wherein said tetracycline derivative is a tetracycline of the formulae selected from the group consisting of:

**Structure A** ——— **or** ——— **Structure B** **or**

**Structure C** ——— **or** ——— **Structure D**



wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, ~~mono(lower alkyl) amino~~, halogen, ~~di(lower alkyl) amino~~, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

R6 and R5 are selected from the group consisting of hydrogen and hydroxyl;

R8 is selected from the group consisting of hydrogen and halogen;

R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, ~~mono(lower alkyl) amino~~, halogen, diazonium, ~~di(lower alkyl) amino~~ and RCH(NH<sub>2</sub>)CO;

R is hydrogen ~~or lower alkyl~~;

and pharmaceutically acceptable and unacceptable salts thereof; with the following provisos:

when either R7 and R9 are hydrogen then R8 must be halogen; and

when R6-a, R6, R5 and R9 are all hydrogen and R7 is hydrogen, amino, nitro, halogen, dimethylamino or diethylamino, then R8 must be halogen; and

when R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl, and R7 is hydrogen, amino, nitro, halogen or diethylamino, then R8 is halogen; and

when R6-a is methyl, R6 is hydroxyl, R5, R7 and R9 are all hydrogen, then R8 must be halogen; and

when R6-a, R6 and R5 are all hydrogen, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

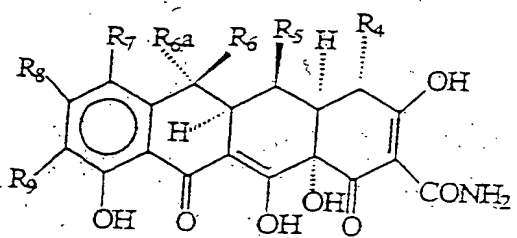
when R6-a is methyl, R6 is hydrogen, R5 is hydroxyl, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

when R6-a is methyl, R6, R5 and R9 are all hydrogen and R7 is cyano, then R8 must be halogen.

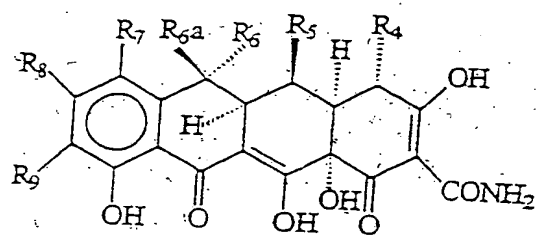
Claim 16 (currently amended)      A method according to Claim 1, wherein said tetracycline derivative is a tetracycline compound of the formulae selected from the group consisting of:

~~Structure E~~ ——— ~~or~~ ——— ~~Structure F~~ ~~or~~

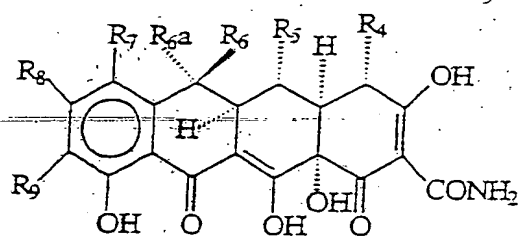
~~Structure G~~ ——— ~~or~~ ——— ~~Structure H~~



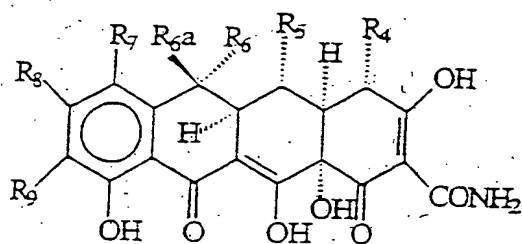
Structure E



Structure F



Structure G



Structure H

wherein

R7 is selected from the group consisting of hydrogen, amino, nitro, ~~mono(lower alkyl)amino~~, halogen, and ~~di(lower alkyl)amino~~, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

R6 and R5 are selected from the group consisting of hydrogen and hydroxyl;

R4 is ~~selected from the group consisting of NOH, N-NH-A, and NH-A,~~

~~where A is a lower alkyl group;~~

R8 is selected from the group consisting of hydrogen and halogen;

R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, ~~mono(lower alkyl)amino~~, halogen, ~~di(lower alkyl)amino~~ and RCH(NH<sub>2</sub>)CO;

R is hydrogen ~~or lower alkyl~~;

and pharmaceutically acceptable and unacceptable salts thereof; with the following provisos:

when R4 is NOH, N-NH-alkyl or NH-alkyl and R7, R6-a, R6, R5, and R9 are all hydrogen, then R8 must be halogen; and

when R4 is NOH, R6-a is methyl, R6 is hydrogen or hydroxyl, R7 is halogen, R5 and R9 are both hydrogen, then R8 must be halogen; and

when R4 is N-NH-alkyl, R6-a is methyl, R6 is hydroxyl and R7, R5, R9 are all hydrogen, then R8 must be halogen; and

when R4 is NH-alkyl, R6-a, R6, R5 and R9 are all hydrogen, R7 is hydrogen, amino, ~~mono(lower alkyl)amino~~, halogen, ~~di(lower alkyl)amino~~ or hydroxyl, then R8 must be halogen; and

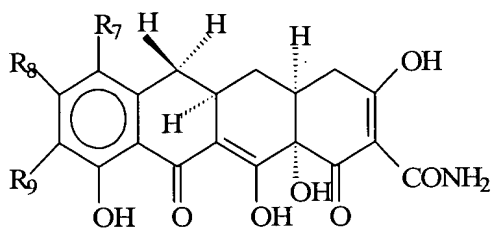
~~when R4 is NH-alkyl, R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl, and R7 is mono(lower alkyl)amino or di(lower alkyl)amino, then R8 must be halogen; and~~

when R4 is NH-alkyl, R6-a is methyl, R6 is hydroxy or hydrogen and R7, R5, and R9 are all be hydrogen, then R8 must be halogen.

Claim 17 (currently amended): A method according to Claim 1, wherein said tetracycline derivative is a 4-dedimethylaminotetracycline compound having general formulae (I) through (IV):

#### **General Formula (I)**

##### **Structure I**



Structure I

wherein: R7, R8, and R9 taken together in each case, have the following meanings:

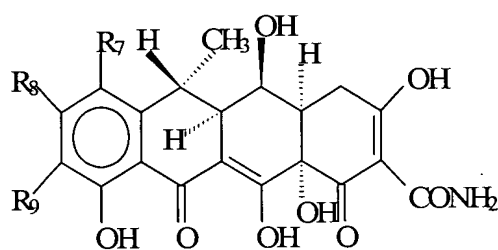
R7	R8	R9
azido	hydrogen	hydrogen
dimethylamino	hydrogen	azido
hydrogen	hydrogen	amino
hydrogen	hydrogen	azido
hydrogen	hydrogen	nitro
dimethylamino	hydrogen	amino
acylamino	hydrogen	hydrogen
hydrogen	hydrogen	acylamino
amino	hydrogen	nitro
hydrogen	hydrogen	(N,N-dimethyl)glycylamino
amino	hydrogen	amino
hydrogen	hydrogen	ethoxythiocarbonylthio
dimethylamino	hydrogen	acylamino
dimethylamino	hydrogen	diazonium
dimethylamino	chloro	amino
hydrogen	chloro	amino
amino	chloro	amino
acylamino	chloro	acylamino
amino	chloro	hydrogen
acylamino	chloro	hydrogen
mono alkylamino	chloro	amino
nitro	chloro	amino
dimethylamino	chloro	acylamino
dimethylamino	chloro	dimethylamino

and

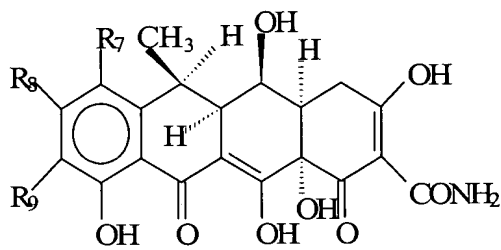
**General Formula (II)**

**Structure J** — or — **Structure K** or

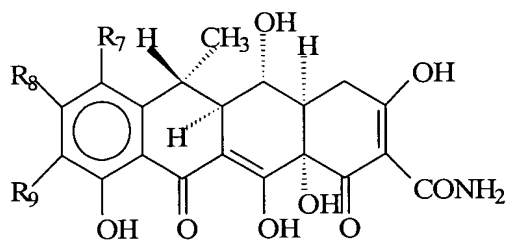
**Structure L** — or — **Structure M**



Structure J

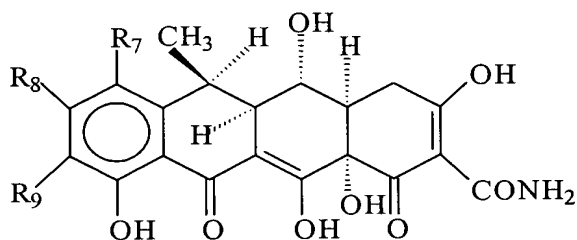


Structure K



Structure L





Structure M

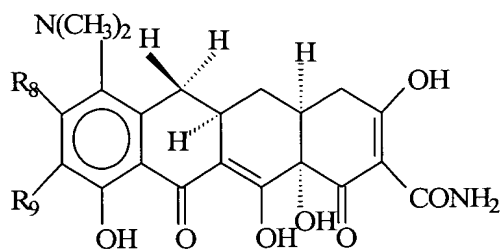
wherein: R7, R8, and R9 taken together in each case, have the following meanings:

R7	R8	R9
azido	hydrogen	hydrogen
dimethylamino	hydrogen	azido
hydrogen	hydrogen	amino
hydrogen	hydrogen	azido
hydrogen	hydrogen	nitro
dimethylamino	hydrogen	amino
acylamino	hydrogen	hydrogen
hydrogen	hydrogen	acylamino
amino	hydrogen	nitro
hydrogen	hydrogen	(N,N-dimethyl)glycylamino
amino	hydrogen	amino
hydrogen	hydrogen	ethoxythiocarbonylthio
dimethylamino	hydrogen	acylamino
hydrogen	hydrogen	diazonium
hydrogen	hydrogen	dimethylamino
diazonium	hydrogen	hydrogen
ethoxythiocarbonylthio	hydrogen	hydrogen
dimethylamino	chloro	amino
amino	chloro	amino
acylamino	chloro	acylamino
hydrogen	chloro	amino
amino	chloro	hydrogen
acylamino	chloro	hydrogen
mono alkyl amino	chloro	amino
nitro	chloro	amino

and

**General Formula (III)**

**Structure N**

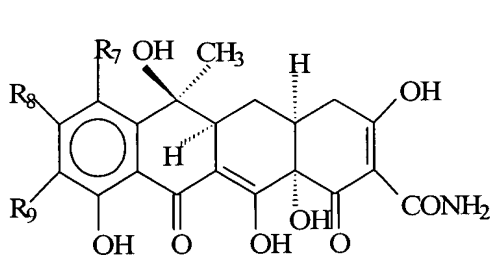


Structure N

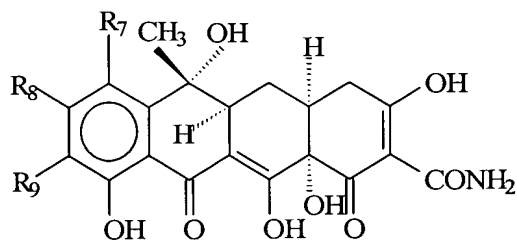
wherein: R8 is hydrogen or halogen and R9 is selected from the group consisting of nitro, (N,N-dimethyl)glycylamino, and ethoxythiocarbonylthio; and

**General Formula (IV)**

**Structure O** — or — **Structure P**



Structure O



Structure P

wherein: R7, R8, and R9 taken together in each case, have the following meanings:

R7	R8	R9
amino	hydrogen	hydrogen
nitro	hydrogen	hydrogen
azido	hydrogen	hydrogen
dimethylamino	hydrogen	azido
hydrogen	hydrogen	amino
hydrogen	hydrogen	azido
hydrogen	hydrogen	nitro
bromo	hydrogen	hydrogen
dimethylamino	hydrogen	amino
acylamino	hydrogen	hydrogen
hydrogen	hydrogen	acylamino
amino	hydrogen	nitro
hydrogen	hydrogen	(N,N-dimethyl)glycylamino
amino	hydrogen	amino
diethylamino	hydrogen	hydrogen
hydrogen	hydrogen	ethoxythiocarbonylthio
dimethylamino	hydrogen	methylamino
dimethylamino	hydrogen	acylamino
dimethylamino	chloro	amino
amino	chloro	amino
acylamino	chloro	acylamino
hydrogen	chloro	amino
amino	chloro	hydrogen
acylamino	chloro	hydrogen
mono alkyl amino	chloro	amino
nitro	chloro	amino

and pharmaceutically acceptable and unacceptable salts thereof.

Claims 18-34 (cancelled).

Claim 35: (currently amended): ~~A method according to Claim 7 of reducing the~~  
risk of cataract development in a mammal comprising administering to the mammal a  
~~wherein said antimicrobial tetracycline is administered~~ in an amount that is effective to  
 reduce the risk of cataract development in a mammal but has substantially no antibacterial  
 activity.

Claim 36 (cancelled).

Claim 37 (new): A method according to Claim 35, wherein said tetracycline is administered systemically.

Claim 38 (new): A method according to Claim 37, wherein said tetracycline is administered systemically by a controlled release delivery system.

Claim 39 (new): A method according to Claim 35, wherein said tetracycline is administered orally.

Claim 40 (new): A method according to Claim 35, wherein said tetracycline is administered topically.

Claim 41 (new): A method of reducing the risk of cataract development in a mammal comprising administering to the mammal an effective amount of minocycline.

Claim 42 (new): A method according to Claim 41, wherein said minocycline is administered systemically.

Claim 43 (new): A method according to Claim 42, wherein said minocycline is administered systemically by a controlled release delivery system.

Claim 44 (new): A method according to Claim 41, wherein said minocycline is administered orally.

Claim 45 (new): A method according to Claim 41, wherein said minocycline is administered topically.

Claim 46: (new): A method according to Claim 41 wherein said minocycline is administered in an amount that is effective to reduce the risk of cataract development in a mammal but has substantially no antibacterial activity.

Claim 47 (new): A method of reducing the risk of cataract development in a mammal comprising administering to the mammal an effective amount of doxycycline.

Claim 48 (new): A method according to Claim 47, wherein said doxycycline is administered systemically.

Claim 49 (new): A method according to Claim 48, wherein said doxycycline is administered systemically by a controlled release delivery system.

Claim 50 (new): A method according to Claim 47, wherein said doxycycline is administered orally.

Claim 51 (new): A method according to Claim 47, wherein said doxycycline is administered topically.

Claim 52: (new): A method according to Claim 47 wherein said doxycycline is administered in an amount that is effective to reduce the risk of cataract development in a mammal but has substantially no antibacterial activity.

Claim 53 (new): A method of reducing the risk of cataract development in a mammal comprising administering to the mammal an effective amount of tetracycline wherein said tetracycline is administered systemically or orally.